Diurnal changes in total circulating magnesium and its subfractions in orally and parenterally substituted and unsubstituted patients[1]

B. Zirm, G. Dreißger, E. Feyrer, H. Eisner, G. Penka, D. Heidinger, S. Porta

Zusammenfassung

In 3 Patientengruppen (n1 = 45, n2 = 45, n3 = 10) wurden Konzentrationen von ionisiertem und totalem Magnesium im Blut um 7 Uhr morgens, um 1 Uhr mittags und um 18 Uhr abends gemessen, der Anteil der gebundenen Fraktion zu diesen Zeitpunkten wurde aus den Meßwerten berechnet. Die 2. Gruppe wurde oral mit 360 mg Magnesiumzitrat substituiert, die 3. Gruppe mit 800 mg Magnesiumsulphat parenteral, unmittelbar nach der morgendlichen Magnesiummessung um 7 Uhr, behandelt.

Es zeigte sich, daß in Gruppe 1 das totale Magnesium signifikant bis um 1 Uhr abfiel, wonach es stabil blieb. Dieser Abfall ist besonders auf die Verringerung der gebundenen Fraktion zurückzuführen.

In der oral substituierten Gruppe 2 nahm das totale Magnesium (hier wiederum vorwiegend die gebundene Fraktion) bis 1 Uhr signifikant zu, um dann zu stagnieren.

In der kleinen parenteral substituierten Gruppe nahm die Magnesiumkonzentration (ebenfalls vorwiegend aufgrund der Veränderung der gebundenen Fraktion) bis 6 Uhr abends stetig und signifikant zu.

Es wird versucht, das Verhalten aller 3 Gruppen mit ein und derselben Hypothese zu erklären: Magnesiumumsatz in den Organen soll demnach von der Menge des zirkulierenden Magnesiums abhängen, so daß erhöhter Magnesiumumsatz der Organe und daher Magnesiumrezirkulation ins Blut durch hohe Magnesiumsupplementation erleichtert wird. Stagnation bei niedrigen Magnesiumwerten während des Nachmittags in der nicht substituierten Gruppe könnte so mit erniedrigtem Organumsatz durch niedrige Nachschubraten erklärt werden. Prinzipiell fällt die Magnesiumkonzentration während des Tagesverlaufes und muß während der ruhigeren Nachtstunden wieder ergänzt werden.

Medical Department, Landeskrankenhaus Bad Radkersburg, Institute of Applied Stress Research, Bad Radkersburg, Hauptplatz 2-4, Austria

[1] Part of the data has been preliminary presented at the joint German, Austrian and Swiss Magnesium Symposium in Berlin, 1996.

Summary

In 3 groups of patients (n1 = 45, n2 = 45 and n3 = 10) ionized and total magnesium concentrations in blood were measured at 7 a.m., 1 p.m. und 6 p.m. and the amount of the bound fraction was calculated. Group 2 was substituted with 360 mg magnesium orally and group 3 with 800 mg magnesium parenterally immediately after the morning measurement. It turned out, that in group 1 total magnesium, especially from the bound group fell significantly until 1 p.m. and remained rather constant afterwards.

In the orally substituted group 2 magnesium (again mainly the bound fraction) increased up to 1 p.m. and stagnated afterwards.

In the small parenterally substituted group total magnesium, still mainly due to alterations of the bound fraction, was increased at 1 p.m. and even more and still significantly so at 6 p.m.

The behaviour of all 3 groups has been tried to explain with one and the same hypothesis: that magnesium turnover in organs can be regulated by circulating magnesium, so that increased turnover and magnesium recirculation into the blood stream can be facilitated by high magnesium supplementation. Stagnation at lower magnesium values during the afternoon could then be explained by turnover decrease due to low support rates. However, levels of circulating magnesium fall during the daytime and will have to be replenished during the less active nightly hours.

Introduction

Changes in circulating total, ionized and bound magnesium concentrations throughout the day have been checked in magnesium substituted (orally and parenterally) and unsubstituted male and female probands.

The reason was, that on the one hand daily magnesium uptake is supposed to be generally insufficient and is therefore to be supplemented (*Emsenhuber* et al. 1990, *Classen* et al. 1995) and on the other hand magnesium should be liberated from soft tissue organs during the day relative to the intensity of ATP - ADP reactions (*Porta* et al. 1994), which usually would be much more pronounced during daytime strains than during the more restful nightly hours.

Thus characteristic diurnal changes of the total circulating magnesium and its subfractions in unsubstituted persons appeared to be feasible. If this holds true, magnesium substitutions may show their own idiosyncratic courses, both on top of the diurnal changes, as well as dependent upon their being given orally or parenterally. Consequently, certain modes of magnesium substitution may eventually suggest themselves.

Material and methods

100 probands with the average age of 51 (between 22 und 76) were randomly distributed into two groups: Group 1 without substitution, 23 females, 22 males, Group 2 with an oral substitution of 365 mg magnesium 22 females, 23 males and Group 3, consisting of 5 female und 5 male probands, substituted with 800 mg magnesium parenterally.

Inclusion criteria: Group 1: Total serummagnesium above 0.8 mmol/l, Group 2: Total serummagnesium of 0.8 mmol/l or below, Group 3: Parenteral magnesium because of cardial indication, base values between 0.76 and 0.94.

Magnesium was given both orally (magnesium citrate) and parenterally (magnesium sulphate) between 7 and 8 a.m. and blood samples were drawn at 7 a.m. (before substitution), at 1 p.m. and at 6 p.m.

Free (ionized) magnesium was determined by the electrolyte analyzer AVL 988-4 (AVL Graz, Austria). Determination of total serum magnesium was carried out

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by the photometric Greiner 450 method using xylidylblue with a highly significant linear correlation to the Kodak method. The bound fraction of magnesium was calculated from the ionized and total fractions (*Porta* et al. 1994).
After ascertaining normal distribution, paired *t*-tests were applied for establishing possible significant differences in circulating magnesium concentration in the time course of the experiment (*Köhler* et al. 1996).

Results

In the orally substituted, as well as in the parenterally substituted group, no signs of unwanted side effects, e. g. diarrhoea, have been reported. Oral magnesium has been diluted in 0.5 l of water and the patients were asked to drink particularly slowly.

1. Non substituted group (tab. 1):
   Total magnesium was significantly lower at 1 p. m. than at 7 a. m. At 6 p. m. total magnesium was still rather low, but not significantly different from the 1 p. m. values. The ionized subfraction fell from 0.59 mM to 0.55 mM (−8 %), while the bound subfraction fell from 0.35 mM to 0.30 mM (−16 %).
2. Orally substituted group (tab. 2):
   Total magnesium and its subfractions increased significantly between 7 a. m. and 1 p. m. and stagnated afterwards.
   The ionized fraction increased from 0.48 mM to 0.53 mM (+10 %), the bound fraction from 0.25 mM to 0.31 mM (+22 %).
3. Parenterally substituted group (tab. 3):
   Here the total circulating magnesium increased steadily and significantly from 7 a. m. to 6 p. m., which is due to the striking increase of the bound fraction from 0.26 mM to 0.45 mM at 1 p. m. and further to 0.5 mM (+95 %) at 6 p. m.

Tab. 1: Patients without substitution
* $p<0.05$, ** $p<0.001$
against 7 a.m.

	Mean ± SEM, 7 a.m.	Mean ± SEM, 1 p.m.	Mean ± SEM, 6 p.m.
Mg total	0.934 ± 0.01	0.857 ± 0.011 **	0.866 ± 0.012 **
Mg ionized	0.585 ± 0.008	0.563 ± 0.007 **	0.553 ± 0.009 *
Mg bound	0.346 ± 0.009	0.299 ± 0.008 *	0.303 ± 0.011 *

Tab. 2: Patients with oral substitution (360 g Magnesium)
* $p<0.05$, ** $p<0.001$
against 7 a.m.

	Mean ± SEM, 7 a.m.	Mean ± SEM, 1 p.m.	Mean ± SEM, 6 p.m.
Mg total	0.727 ± 0.008	0.836 ± 0.011 **	0.844 ± 0.010 **
Mg ionized	0.484 ± 0.009	0.524 ± 0.010 *	0.533 ± 0.009 **
Mg bound	0.250 ± 0.010	0.313 ± 0.008 **	0.312 ± 0.008 *

Tab. 3: Patients with parenteral substitution (800 mg Magnesium)
* $p<0.05$, ** $p<0.001$
against 7 a.m.
$^{+}p<0.05$, $^{++}p<0.001$
against 1 p.m.

	Mean ± SEM, 7 a.m.	Mean ± SEM, 1 p.m.	Mean ± SEM, 6 p.m.
Mg total	0.805 ± 0.007	1.136 ± 0.025 **	1.180 ± 0.009 ** $^{+}$
Mg ionized	0.544 ± 0.008	0.691 ± 0.025 *	0.682 ± 0.003 **
Mg bound	0.261 ± 0.007	0.445 ± 0.009 **	0.498 ± 0.009 ** $^{++}$

Discussion

The significant decrease of total magnesium in the non substituted group took place mainly during the morning hours and is chiefly due to the pronounced fall of the bound fraction. That there is no observable increase in the ionized fraction could be mainly due to the fact, that the long measuring intervals do not allow observation of the rather quick changes in ionized serum magnesium (*Porta* et al. 1995), which, in time seems to be taken up into the bound fraction, thus leading to its steady increase (*Zirm* et al. 1995). The afternoons steady state after the early decrease must be followed by a nightly replenishment, mainly of the circulating, bound fraction out of tissue magnesium reserves. This afternoon steady state could be due to concentration-dependent regulation system, which may be controlled both stoichiometrically or hormonally.
Orally substituted magnesium increases circulating total magnesium mainly by increasing its bound – and not the more stable ionized fraction (bound fraction +22 %, ionized fraction +10 %). Those changes are, as already mentioned above, also observable mostly during the morning hours.
In parenterally substituted patients however, steady increases in both the total and the bound fraction could be observed even until 6 p. m., while the increase of the ionized fraction did not commence beyond the 1 p. m. mark.
The parenterally given amount at 7 a. m. is obviously able to increase the bound fraction for at least 11 hours to come, without increasing the ionized fraction at all.
If we assume transitory peaks of different size after oral substitution (360 mg) or after bolus injection (800 mg) and a subsequent decrease of circulating magnesium, the fact of a significantly increased stable magnesium level after oral substitution or steady and significant increase of circulating magnesium in the parenterally substituted group in the afternoon hours invites comment:
A feasible explanation may be, that during the morningly decrease of the peak values a comparatively high amount of magnesium has been taken up into bone and other organs and is returned in due

course into the blood stream again. This may lead to increased circulating exchange between bloodstream and organs, creating – concentration dependent – either a steady state at increased levels during the afternoon, or even an increase.

If this would be true, it must mean, that magnesium substitution also increases the magnesium turnover of the organs. If then the magnesium turnover of organs could be influenced by the magnesium status, magnesium loss could lead to lower turnover, which could explain the steady afternoon values of the non supplemented group after the morningly decrease.

Magnesium substitution should then take into account, that organ magnesium turnover of substituted persons may be increased. Also the nightly replenishing mechanism, though poorly understood, may be influenced by magnesium application in the evening.

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Correspondence to:
Sepp Porta, Institute of Applied Stress Research, Bad Radkersburg, Hauptplatz 2–4, A-8490, Austria.